REMARKS

Claims 1, 5, 6, 11, 20 and 22-31 are pending in the instant application. Claims 1, 5, 6, 11, 20 and 22-31 have been rejected. Claims 1, 23, 24, 25, 26, 28 and 29 have been amended. Claims 5, 6, 20, 27 and 30-31 have been canceled in light of the amendments to claim 1. New claim 32 specifying the penetration rate of bisoprolol through the skin to be between 4 and 300 $\mu g/h \cdot cm^2$ in accordance with teachings throughout the specification has been added. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of the amendments and the following remarks.

Rejection of Claims under 35 U.S.C. 103(a)

The rejection of claims 1, 5, 6, 11, 20 and 22-31 under 35 U.S.C. 103(a) as being unpatentable over Modamio et al. (Int. J. Pharmaceutics 1998 173:141-148) in view of Hirano et al. (U.S. Patent 6,495,159), Higo et al. (U.S. Patent 5,866,157), and Heller, further evidenced by Walters (Transdermal Drug Delivery, 1989, New York, NY, pp 97-246), has been maintained.

Applicants respectfully traverse this rejection.

In an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to recite an adhesive patch consisting essentially of a release liner, a drug-

containing pressure-sensitive adhesive layer comprising bisoprolol or a pharmaceutically acceptable salt thereof, styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate·vinyl acetate·acrylic acid copolymer, isopropyl myristate, sodium acetate, a plasticizer and a tackifying resin, and a backing layer contacting the drug-containing pressure-sensitive adhesive layer one a side opposite to the release liner. Further Applicants have added new claim 32 specifying the penetration rate of bisoprolol through the skin to be between 4 and 300 $\mu g/h \cdot cm^2$ in accordance with teachings throughout the specification

The cited combination of art does not teach or suggest a patch with the recited components.

As acknowledged by the Examiner at page 6, paragraph 16 of the Final Rejection mailed May 10, 2010, Modamio does not teach or suggest the limitations of the instant claimed invention of:

a patch possessing an adhesive layer comprising 2-ethylhexyl acrylate-butyl acrylate-acrylic acid copolymer;

a rate of penetration of bisoprolol through the skin as 4 and 300 $\mu g/h \cdot cm^2$ as set forth in claim 32; or

isopropyl myristate.

Hirano also fails to teach or suggest the limitations of the instant claimed invention. Hirano et al. does not teach or suggest an adhesive patch consisting essentially of a release liner, a drug-containing pressure-sensitive adhesive layer and a backing layer contacting the drug-containing pressure-sensitive adhesive layer one a side opposite to the release liner as now claimed. In fact, Hirano specifically distinguishes their invention the instant claimed matrix formulation. Instead, the percutaneous therapeutic apparatus of Hirano requires as an essential component an additional medicine storage layer between the backing layer, the medicine releasing layer and the adhesive layer. Further, Hirano is silent with respect to a drug-containing pressure sensitive adhesive layer comprising styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate·vinyl acetate·acrylic acid copolymer, a plasticizer and a tackifying resin as now claimed.

Higo et al. also does not teach or suggest all limitations of the instant claimed invention. This reference is silent with respect to bisoprolol or a pharmaceutically acceptable salt thereof. Higo et al. also

does not specifically disclose use of 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer as claimed.

Finally, Heller et al. is directed to methods of percutaneously administering physiological agents to the skin. Heller et al. is silent about an adhesive patch, and consequently an adhesive layer. While Heller et al. mentions isopropyl myristate, it is not used in combination with bisoprolol or a pharmaceutically acceptable salt thereof, styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer, sodium acetate, a plasticizer and a tackifying resin as claimed. In addition, although Heller et al. mentions beta-blockers pindolol and propranolol, these are structurally different from bisoprolol. Thus, Heller et al. also does not teach or suggest all limitations the claimed invention.

Accordingly, since the cited combination of references does not teach or suggest a drug-containing pressure-sensitive adhesive layer comprising bisoprolol or a pharmaceutically acceptable salt thereof, styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate·vinyl acetate·acrylic acid copolymer, isopropyl myristate, sodium acetate, a plasticizer and a tackifying

resin as now claimed and only Higo et al. relates generally to matrix patch formulations of a release liner, a drug-containing pressure-sensitive adhesive layer and a backing layer contacting the drug-containing pressure-sensitive adhesive layer one a side opposite to the release liner without any teaching or suggestion of bisoprolol, it would not have been obvious for a skilled artisan to accomplish an adhesive patch as now claimed.

Further, it is impossible to predict from the cited teaching usability of an adhesive layer comprising bisoprolol in combination with styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer, isopropyl myristate, sodium acetate, a plasticizer and a tackifying resin as not only Modamio et al. but also Hirano et al., Higo et al. and Heller et al. fail to suggest such a combination. With respect to the use of 2-ethylhexyl acrylate· vinyl acetate· **acrylic acid** copolymer as claimed, this is not obvious. While Hirano et al. discloses the use of 2-ethylhexyl acrylate· vinyl acetate copolymer (Example 1), Comparative Example 2 in the present specification shows that the adhesive patch comprising 2-ethylhexyl acrylate· vinyl acetate copolymer instead of 2-ethylhexyl acrylate·

vinyl acetate· **acrylic acid** copolymer as claimed exhibits inferior adhesive properties and drug-content stability compared to the instantly claimed adhesive patch. Specifically, the adhesive patch of the present invention was graded as "A" in the adhesive force test because it met all of the following criteria: 300 gF or more by means of a probetack tester, 150 gF/cm or more by means of a peel measuring instrument, and 500 seconds or more until a patch loaded with 500 gF are detached from a surface by means of a creep measuring instrument. This means that the adhesive patch of the present invention is considered to remain adhered to the skin and the adhesive patch can be removed from the skin without leaving any adhesive deposit on the skin after 24-hour adhesion of the adhesive patch to the skin. In contrast, the adhesive patch of Comparative Example 2, which was graded as "B" in the adhesive force test, did not meet at least one of the above-mentioned criteria. These results indicate that although Hirano et al. may disclose the use of 2-ethylhexyl acrylate· vinyl acetate copolymer, which does not comprise acrylic acid, the improvement in adhesive properties and drug-content stability by the use of a copolymer having a specific combination of the monomers 2-ethylhexyl acrylate, vinyl

acetate and acrylic acid, as claimed, could not have been predicted by a skilled artisan. Nor would it have been expected by a skilled artisan to use 2-ethylhexyl acrylate· vinyl acetate copolymer from Modamio et al., Higo et al. and Heller et al., since none of these references specifically disclose 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer. Furthermore, the matrix-type adhesive patch of the present invention performed excellent penetration of drug (bisoprolol or a pharmaceutically acceptable salt thereof), excellent adhesiveness, no crystal deposition and excellent drug-content stability by containing bisoprolol or a pharmaceutically acceptable salt thereof, styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer, isopropyl myristate, and sodium acetate, a plasticizer and a tackifying resin in the adhesive layer. Since the percutaneous therapeutic apparatus taught by Hirano et al. is a reservoir type and does not comprises a drug together with styrene-isoprene-styrene block copolymer and/or polyisobutylene, 2-ethylhexyl acrylate· vinyl acetate· acrylic acid copolymer, a plasticizer and a tackifying resin in the adhesive layer, a person skilled in the art would not have expected all the above-mentioned effects by containing

all the above-mentioned components in an adhesive layer of a matrix-type adhesive patch.

Accordingly, the structure and ingredients of the adhesive patch of the present invention and the advantageous effects thereof are not obvious from the cited references.

Withdrawal of this obviousness rejection is therefore respectfully requested.

Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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